REMARKS

I. Generally

By this Amendment and Response, Applicants have amended Claims 1, 3, and 5-7; cancelled Claims 4 and 9-12; and added Claims 13-25. Thus, Claims 1-3, 5-8, and 13-25 are pending.

II. Rejection of Claims 1, 5-7, and 9 under 35 U.S.C. §103(a)

Claims 1, 5-7, and 9 have been rejected under 35 U.S.C § 103(a) over Ladner et al. (USPN 5,962,246) ("the Ladner patent") in view of Lundquist et al. (J.Biol.Chem., Vol. 272, No. 34, pp.21408-21419, 1997). Claim 9 is cancelled. To the extent that the rejection is applied to the amended claims 1 and 5-7, Applicants respectfully traverse.

Obviousness has three components: First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Applicants respectfully submit that neither the Ladner patent, nor Lundquist, alone or in combination, teach or suggest all of the components of the claims under consideration. Claims 1 and 22 are the only independent claims under consideration in the instant application, both of which both clearly require the following:

a. screening a profile of four specific cells types after exposure to a test compound; and

b. measuring multiple parameters within each cell type, wherein defined outcomes, including among other metrics, the amount of uracil present in the DNA and dUTP levels in the cells, indicate

that the compound induces uracil misincorporation. Neither the Ladner patent nor Lundquist contain these limitations.

On the bottom of page 4, the Office Action asserted that "Ladner et al. teach a method for determining if a test compound induces uracil misincorporation into DNA ... ." While the Ladner patent has broad applicability, its teachings do not extend to a method for determining if a test compound induces uracil misincorporation into DNA as taught in the present invention. The Ladner patent describes (1) a method for determining "the proliferation status of a cell using dUTPase as a marker," (column 4, lines 41-43) and (2) a method for determining the likely response of a cancer cell to an antineoplastic agent by tracking "the level of dUTPase of a cancer cell" (column 4, line 62 through column 5, line 8). A drop in the level of dUTPase in a cell may be positively correlated, as the Ladner patent suggests (column 4, line 65 through column 5, line 1), with an increase in uracil misincorporation in DNA. However, it is not necessarily a definitive marker for uracil misincorporation due to the inhibition of thymidylate metabolism because there are several other enzymes that function downstream from dUTPase to enable or prohibit uracil misincorporation into DNA, such as, uracil-DNA glycosylase (UDG). A non-functional UDG would yield stable uracil integration into DNA, a condition that corresponds to a different cellular phenotype than uracil misincorporation and the aberrant uracil-DNA metabolism resulting in part from a functional UDG. Therefore, the parameters measured in the methods described by the Ladner patent do not teach the same methods for determining uracil misincorporation into DNA described in claims 1 and 22 of the present invention.

Similarly, the Office Action asserted the Ladner patent teaches that the present method comprises "...measuring cell growth or proliferation or viability or measuring incorporation of uracil (dUTP) or amount of dUTPase," and " ...interpreting the measured features wherein presence or absence of uracil in DNA in each of the cell types is indicative of the test compound inducing uracil

misincorporation into DNA " (Office Action page 3, line 12-16). Again, this teaching does not encompass measuring the metrics of presence or absence of uracil in DNA, dUTP levels and optionally, cell cycle checkpoint arrest. Further, measuring levels of dUTPase and the dUTP/UMP cellular equilibrium is not necessarily equivalent to measuring uracil incorporation in DNA, which depends on the combined activity of multiple enzymes downstream from dUTPase, including UDG.

As the Office Action correctly point outs, the Lundquist et al only describe (1) a method for cloning and transforming bacteria cells, which over express uracil-DNA glycosylase (Ung) and cells, which express uracil-DNA glycosylase inhibitor protein (Ugi), and (2) the interaction of the Ung and Ugi and the ability of Ugi to inhibit Ung activity. Lundquist does not in any way teach or suggest a method for determining if a test compound induces uracil misincorporation into DNA or using the transformed cells in a process relating to uracil misincorporation.

Applicants respectfully assert that an ordinary skilled artisan would not be motivated upon reading either Ladner or Lundquist to combine the methods taught in Ladner and Lundquist, because neither method teach nor suggest using the four cell types to screen for the metrics as defined in Claims 1 and 22.

III. Rejection of Claims 2-4, 8 and 10 under 35 U.S.C. §103(a)

Claims 2-4, 8 and 10 have been rejected under 35 U.S. § 103(a) over Ladner et al. (USPN 5,962,246) in view of Lundquist et al. (J.Biol.Chem., Vol. 272, No. 34, pp.21408-21419, 1997) and further in view of Pearlman et al (USPN 6,322,991). Claims 4 and 10 have been cancelled. To the extent that the rejection can be applied to the amended claims 2, 3 and 8 Applicants respectfully traverse.

Claims 2, 3 and 8 of the present application all depend from claim 1, therefore, all of the foregoing arguments articulated above in response to the rejection of claim 1 are applicable here.

Applicants further submit that it would not have been obvious to a person of ordinary skill in the art to combine the target host cells taught by Pearlman et al with the methods taught by the Ladner patent and Lundquist et al to achieve the method of present invention. The Office Action correctly points out that Pearlman teaches "a method to screen for dUTPase inhibitors in organisms comprising Saccharomyces cerevisiae" (Office Action, page 5, lines 20-21). However, the Office Action then claims that combining the methods taught by the Ladner patent and Pearlman et al would achieve an "expected advantage of developing a sensitive method for characterizing uracil misincorporation into DNA." (Office Action, page 6, lines 11-12). However, this is not the case.

A person of ordinary skill in the art would not be motivated to combine Pearlman et al and the Ladner patent to develop the method described by the present invention, because, as described above, the Ladner patent does not teach the method for determining uracil misincorporation into DNA as taught in the present invention, a premise the Office Action relies on (Office Action, page 6, lines 9-10), which is central to this rejection. Pearlman neither teaches the limitation of using the profile of cell types described in claims 1 and 22, one cell type of which overexpresses a uracil-DNA glycosylase, nor the limitation of using the presence of uracil in the DNA of the various cell types exposed to a test compound as an indication for uracil misincorporation in these cells types. Thus, none of references in this obviousness combination teach or suggest the methods of the present application, particularly in light of the amended claims.

Therefore, Applicants respectfully request the withdrawal of both obviousness rejections.

CONCLUSION

The Commissioner is authorized to charge any fees required by the filing of these papers, and to credit any overpayment to Perkins Coie's Deposit Account No. **50-2586**. If anything can be done to further this application, please contact the undersigned at 310-788-9900.

Respectfully submitted,

Perkins Coie LLP

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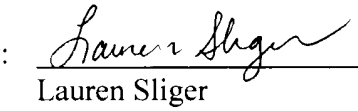
By: 

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